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Metastasis of Carcinoma to the Thyroid Gland *

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THE THYROID gland usually is considered to be an infrequent site of metastatic involvement from primary carcinoma of other organs. This seems odd in view of the fact that the thyroid is one of the most richly arterialized tissues in the body. Metastatic lesions do develop in the thyroid gland in some patients who harbor primary malignant neoplasms in other sites, and, in a few patients, the metastatic lesion may manifest itself clinically as a goiter. This metastasis to the thyroid parenchyma in some patients has been investigated by various workers. Mayo and Schlicke pointed out that, in their study of this phenomenon, most metastatically involved glands were frankly adenomatous in varying degrees. Willis suggested that two factors that might determine the predisposition of altered thyroid tissue to metastatic growths are altered vascular conditions in adenomatous regions favoring the arrest of blood-borne emboli and a lowered iodine and oxygen content in the gland. However, adenomatous glands were the sites of metastatic involvement no more often than were nonadenomatous glands in the consecutive necropsy series reported by Mortensen, Woolner and Bennett.

This report describes all cases of secondary carcinomas of the thyroid gland that were treated surgically or proven by biopsy at the Mayo Clinic from 1907 through 1962. Only 14 surgically proven cases of carcinoma metastatic to the thyroid gland with a tissue diagnosis of the primary neoplasm were encountered. There were two additional cases in which there was a diagnosis of metastatic carcinoma in the thyroid gland but tissue from the primary site of the neoplasm was not obtained.

Cases in which direct invasion of the thyroid by primary tumors of the larynx, pharynx, esophagus, lung, and head occurred are not included in this study.

General Observations

Incidence. Careful postmortem studies by interested pathologists during the past 32 years have revealed metastatic deposits in the gland more frequently than was believed to be the case previously. Rice found

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embolic tumor cells within the thyroid gland in nine of 89 necropsies in cases in which death was caused by malignant tumors. Metastatic lesions of the same type as the cancer that caused the death were found by Hull in ten of 59 thyroid glands taken from persons dying of cancer. Mortensen, Woolner and Bennett demonstrated metastatic lesions in the thyroid glands of 4.9 per cent of patients with demonstrable metastasis at necropsy and Willis reported an incidence of 5.2 per cent in an earlier similar study.

As would be expected, the incidence of metastatic lesions that present clinically as a mass in the thyroid is much lower than that found in series based on necropsy. Weiskittel found one case of hypernephroma with metastasis to the thyroid gland in a review of 10,000 cases of goiter treated by operation. Among the 1,702 thyroidectomies reported by Boys, there was one case of metastatic hypernephroma. Elliott and Frantz summarized the clinical cases of metastatic carcinoma of the thyroid in the literature from 1934 to 1958 and found a total of 58 cases.

Of 20,262 patients who underwent operation on the thyroid at the Mayo Clinic from 1940 through 1961, inclusive, there were ten who had proved malignant disease with metastasis to the thyroid gland. Two more patients seen during this period had had a thyroid operation elsewhere. Pemberton and Bennett found only two such patients among the 45,421 patients who had operations for goiter at this clinic during the period 1892 to 1932, inclusive.

Age and Sex. In the 14 cases reported herein, the average age of the patients was 55.7 years, the youngest patient being 35 and the oldest, 71 years old. This is similar to results of the study by Cope and coworkers in which an average age of 56 years with a range from 39 to 74 years was found.

Eight of the 14 patients were women. The two additional patients, for whom there was no histologic confirmation of the primary tumor, were men.

Location of the Primary Tumor. The primary lesion was hypernephroma in eight cases, adenocarcinoma of the breast in four cases, and adenocarcinoma of the rectum and transitional cell tumor of the urinary bladder in one case each. In the two cases in which the primary disease was not documented histologically, the primary tumor was suspected to be hypernephroma in one and mucus-producing adenocarcinoma of the gastro-intestinal tract in the other on the basis of clinical studies and histologic examination of the metastatic lesions in the thyroid.

Mode of Presentation. A thyroid mass was present in all 14 patients. Four patients complained of a sense of fullness or tightness in the neck, and a change in voice occurred in five patients. Other complaints included difficulty in swallowing, shortness of breath, and stridor.

Thyroid operation followed surgical treatment of the primary neoplasm in 12 cases. In one of these cases, metastatic lesions from a hypernephroma were found in the thyroid 18 years after nephrectomy. In another case, nephrectomy was performed 11 days after resection of the metastatic lesion, in the thyroid, of a hypernephroma. Necrospy one day after thyroid operation revealed hypernephroma in the remaining case.

Case Reports

Four of the cases (no. 1, 2, 4, and 5) in this series have been reported [2, 9, 13] previously and are summarized below. One case (no. 3) was mentioned in an earlier paper by Mayo and Schlicke,[1] but will be reported in detail here since no particulars were given in that report.

Case 1. A 71-year-old man was seen at the Mayo Clinic in June 1918 because of urinary symptoms, including obstruction, of 12 years'

duration (case previously reported by Pemberton and Bennett). The urinary condition improved on a conservative regimen and he was dismissed with the understanding that prostatectomy would be performed in about eight weeks. A symptomless goiter, which had been present for two years, also was noted at that examination.

In November 1918, the patient returned complaining of increasing fullness of the neck, difficulty in swallowing, and dyspnea on exertion. Multiple nodular tumors of the thyroid were palpated and thoracic roentgenograms revealed cardiomegaly and marked congestion of the lung fields.

Double resection of the thyroid with removal of the isthmus was performed in December 1918. Histologic sections of the tissue revealed metastatic hypernephroma. The patient died one day postoperatively in severe respiratory distress, and Grade 2 hypernephroma of both kidneys was found at necropsy.

Case 2. A 35-year-old woman came to this clinic in May 1933 with goiter that had been increasing in size over a two-year period (case previously described by Pemberton and Bennett). Other complaints were nervousness, intolerance to heat, palpitations, and a sense of tightness in the neck.

The left lobe of the thyroid was resected and the pathologic diagnosis was metastatic hypernephroma in a colloid goiter.

An intravenous urogram, nine days later, was suggestive of right renal tumor and right nephrectomy was performed. Grade 2 hypernephroma was found and the patient received a course of x-ray therapy before she was dismissed.

A letter from her local physician revealed that the patient died on May 15, 1943 with *recurrent nodular swelling of the left lobe of the thyroid gland.*

Case 3. A 37-year-old woman registered at this clinic in July 1939 for evaluation of bloody stools. About eight months prior to her arrival, the bleeding had been attributed to hemorrhoids (by a local physician). Two months before admission, she began having eight to 12 bowel movements daily and during the two-month period had lost nine pounds. On proctoscopic examination here, an annular lesion, 6 cm. above the dentate line, was found.

Combined abdominoperineal resection was performed four days after admission and microscopic sections revealed Grade 1 (Broders) adenocarcinoma with involvement of lymph nodes. The patient did well postoperatively and was dismissed in good condition.

Six months later, the patient returned because of severe burning pain with menstruation and was treated for cystic cervicitis. At this time the right lobe of the thyroid gland was found to be enlarged. Shortly thereafter, the right lobe and isthmus of the thyroid was resected and the pathologist reported Grade 1 adenocarcinoma metastatic from the rectum (Fig. 1).

The patient returned, seven months after the thyroid operation, with numerous complaints. Examination at this time revealed a firm, irregular mass in the right sacral fossa and right cul-de-sac,

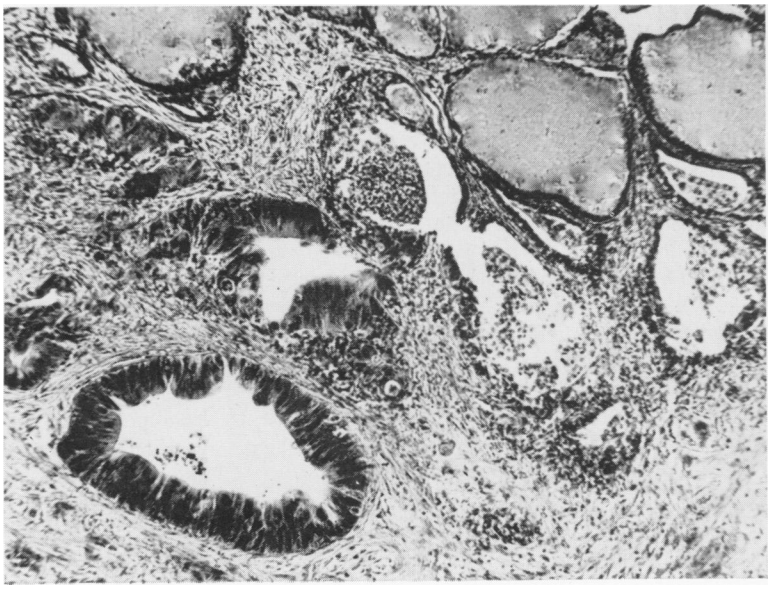

FIG. 1. (Case 3.) Histologic section showing metastasis from adenocarcinoma of the rectum to the thyroid gland (hematoxylin and eosin; × 100).

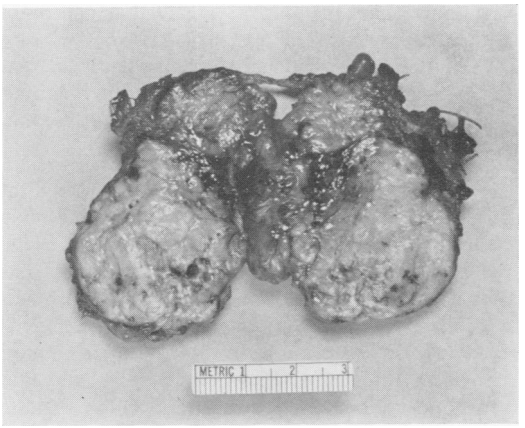

FIG. 2. (Case 4.) Surgical specimen of thyroid tissue containing metastatic lesions from hypernephroma.

irregular firm masses in the thyroid, and consolidation of the upper field of the right lung on roentgenograms. She was sent home to have x-ray therapy to the pelvic area and radium applications to the thyroid. Three months afterward, she died.

Case 4. A 50-year-old man registered at this clinic in August 1935 with a history of kidney trouble of one year's duration (case previously described by Long and Black). Nephrectomy was performed and Grade 2 hypernephroma was found. He was dismissed in good condition after a course of x-ray therapy.

The patient returned in June 1944 because of goiter that had been enlarging over a one year period. Double resection of the thyroid with removal of isthmus was performed and the pathologic report was multicentric, metastatic, Grade 2 hypernephroma. A course of x-ray therapy was given postoperatively.

In July 1952, he returned complaining of hoarseness, fatigue, and a weight loss of 20 pounds. A biopsy, from the left lateral wall of the trachea, showed metastatic hypernephroma. The left lobe of the thyroid was excised and was found to contain metastatic hypernephroma again (Fig. 2).

A tender, irregular nodule appeared in the right upper quadrant of the abdomen one year later and the patient was given a course of x-ray therapy to that region. He died one year afterward, after a massive gastric hemorrhage.

Case 5. A 66-year-old man came to this clinic in March 1952 for evaluation of goiter and hoarseness (case previously described by Beahrs, Ginsberg and Miller). Twenty months prior to his arrival, left nephrectomy for hypernephroma had been done at another hospital.

After examination here, the right lobe and isthmus of the thyroid was resected and the pathologist reported metastatic hypernephroma. An extensive course of x-ray therapy was applied to the neck and mediastinum postoperatively. The patient died in May 1953.

Case 6. A 38-year-old woman was seen here in January 1945, two days after a painless mass in the right breast had been removed at another hospital. The tissue was forwarded here for pathologic review and a diagnosis of Grade 3 adenocarcinoma with associated fibroadenoma was made.

Right radical mastectomy was performed and all nodes in the surgical specimen were reported to exhibit only inflammatory changes. The postoperative course was uneventful.

Thirteen years later, in July 1953, she was readmitted to the hospital because of pain in the right side of the chest, hoarseness, and nonproductive cough. A firm region was palpated in the upper pole of the right lobe of the thyroid and thoracic roentgenograms revealed nodular metastatic lesions in the middle of the left lung. A specimen was removed surgically from the right lobe of the thyroid, and the pathologic report was Grade 4 adenocarcinoma metastatic from the breast. She was then given a course of x-ray therapy.

Letters from the patient's family physician disclosed that numerous bony metastatic lesions developed before her death in June 1957.

Case 7. This 70-year-old man registered at the Mayo Clinic in October 1954 because of a lump in the left side of the neck which had been present for 40 years. He had been asymptomatic since left nephrectomy had been done for hypernephroma in 1936.

After examination here, the left lobe and isthmus of the thyroid was resected (Fig. 3a). Microscopic sections of the tissue revealed metastatic hypernephroma (Fig. 3b). The patient was dismissed in good condition and had no signs of recurrent tumor until May 1961 when multiple, bilateral, nodular metastatic lesions in the lungs and fractures of the left eighth, ninth, and tenth ribs were seen on thoracic roentgenograms. A course of radiotherapy was administered by his local physician with good results. However, one year later the pulmonary lesions were found to have become more extensive and larger, and x-ray therapy at this time was ineffective.

He was last seen here in July 1962 and showed evidence of general deterioration.

Case 8. A 59-year-old woman was seen at this clinic in February 1956 because of swelling in the neck that had appeared one year after thyroid operation elsewhere. She also complained of dyspnea on exertion, hoarseness, anorexia, nausea, a weight loss of 60 pounds, and a choking sensation in her throat. She had undergone right nephrectomy for hypernephroma in 1949, and subtotal thyroidectomy in 1955 because of a firm nodule in the left lobe of the thyroid gland. Gross specimens and slides obtained by both surgical procedures were received here for verification at that time (1955). The thyroid lesion was diagnosed as metastatic hypernephroma and the patient received 20 x-ray treatments at the hospital where the operation had been performed.

Physical examination here disclosed a firm 8 by 19-cm. mass in the thyroid region, right cervical adenopathy, and hepatomegaly to the level of the umbilicus. Multiple metastatic lesions in the left lung were detected on thoracic roentgenograms. At her request, she was dismissed to the care of her family physician.

Case 9. The patient, a 51-year-old woman, came to this clinic in January 1954 because of a mass in the left breast that had been present for three weeks. Left radical mastectomy was performed and multicentric, Grade 3 scirrhous adenocarcinoma, with 13 metastatically involved axillary nodes, was found on microscopic examination of sections of the tissue. She received a course of x-ray therapy before her dismissal from the hospital.

She returned in May 1955 with a small subcutaneous nodule in the right side of the mastectomy incision. It was excised and found to be metastatic Grade 3 adenocarcinoma. Another course of x-ray therapy was administered to the patient.

On subsequent visits there were no problems until December 1957, when a firm, discrete, nontender mass was palpated over the isthmus of the thyroid. Nine days later, the mass had tripled in size and the patient complained of difficulty in swallowing, hoarseness, and stridor. The vocal cords were paralyzed bilaterally and a needle biopsy of the mass revealed Grade 4 adenocarcinoma in the thyroid which was metastatic from the primary neoplasm in the breast. Radiotherapy was begun, but, 11 days after the biopsy had been taken, she suffered an attack of severe inspiratory stridor and became cyanotic. Emergency tracheotomy over a bronchoscope was done and some of the mass overlying the trachea was excised. The tissue had the same histologic characteristics as that obtained by the needle biopsy. Several biopsies which also contained metastatic adenocarcinoma were obtained from the bronchi at the time of bronchoscopy.

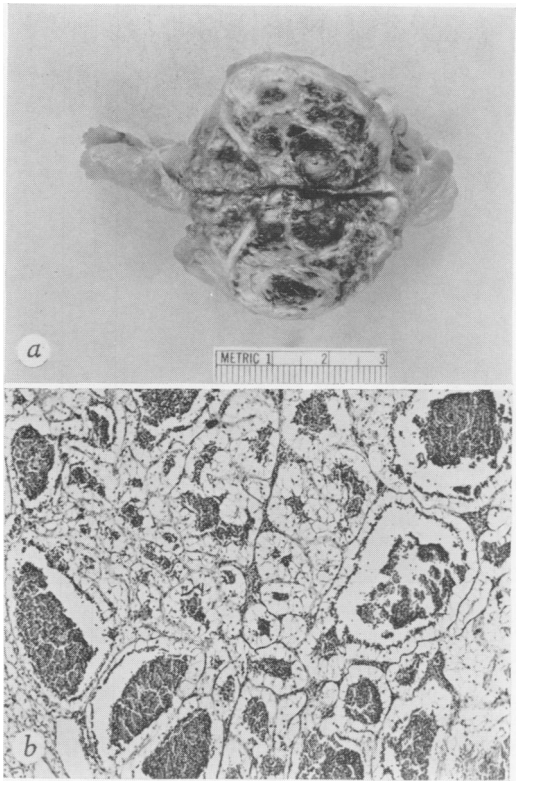

FIG. 3. (Case 7.) *a.* Gross appearance of resected thyroid tissue containing metastatic lesions from hypernephroma. *b.* Typical histologic pattern of hypernephroma evident in a section of tissue removed from the thyroid gland (hematoxylin and eosin; × 90).

Five days later, on May 31, 1958, the patient died after a steady downhill course with fever during the last 36 hours.

Case 10. In October 1956, a 60-year-old man came to this clinic with a chief complaint of passing blood clots on urination. The hematuria had been attributed to cystitis and the patient had been treated with antibiotics in 1954. In 1955, he had had resection of the bladder neck and transplantation of the left ureter at another hospital.

Cystoscopy here revealed a lesion, about the size of a silver dollar, high on the right lateral wall of the bladder which proved to be Grade 4 transitional cell carcinoma. The insertion of 20 radon seeds into the tumor was followed by cobalt-60 therapy to the bladder. A firm 2 by 3-cm. nodule on the left lower lobe of the thyroid was

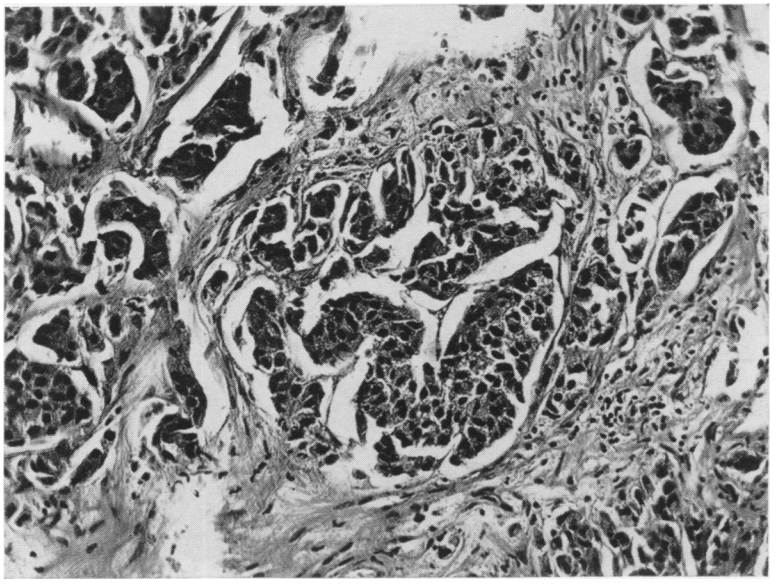

FIG. 4. (Case 10.) Section from thyroid showing metastasis from transitional cell tumor of the urinary bladder (hematoxylin and eosin; × 200).

recorded on general physical examination at this time but surgical therapy was deferred.

There was nothing to suggest recurrence of the tumor in the bladder and there were no changes in the thyroid nodule on return visits. However, in August 1958 thoracic roentgenograms revealed nodular densities in both lung fields. A biopsy of the thyroid nodule was taken with a Silverman needle and the pathologist reported metastatic tumor from the urinary bladder (Fig. 4). Radiotherapy was administered to the patient before he was dismissed from the hospital.

Five months later, the patient died at home.

Case 11. This white woman first was seen here in August 1949 when she was 40 years old. At that time, the terminal part of the ileum, the cecum, the right colon, the right half of the transverse colon, and an apron of omentum were resected because of an annular polypoid intussuscepting Grade 1 mucous adenocarcinoma beginning 18 cm. distal to the ileocecal valve.

In September 1957, right radical mastectomy was performed on the patient after she had presented with a mass in the upper outer quadrant of the right breast. On pathologic examination, Grade 3 scirrhous adenocarcinoma was found but all lymph nodes in the specimen showed only inflammatory changes.

An asymptomatic firm, fixed mass was palpated in the right lobe of the thyroid in December 1960 during a routine visit for re-examination. The right lobe and isthmus of the thyroid was resected, and the right recurrent laryngeal nerve was sacrificed because the carcinomatous mass was found to extend posteriorly, invading the posterolateral wall of the trachea and right anterolateral wall of the esophagus. The pathology report was Grade 4 scirrhous adenocarcinoma metastatic from the breast (Fig. 5). Postoperatively, a course of cobalt-60 therapy was administered before dismissal.

In April 1961, roentgenograms revealed metastatic lesions in the right lung, ribs, and lumbar vertebrae. Bilateral salpingo-oophorectomy was performed and follow-up roentgenographic examinations several months later revealed some decrease in the size of the metastatic lesions. There was no further change on subsequent thoracic and bone roentgenograms and when last seen, in August 1962, the patient was asymptomatic.

Case 12. In April 1961, a 65-year-old woman came to this clinic with a history of having had a lump in the neck for four weeks. Her only other complaint was easy fatigability. She had undergone right nephrectomy for hypernephroma at another hospital in 1947.

On examination, a firm 3 by 4-cm. mass was palpated on the thyroid and thoracic roentgenograms revealed widening of the superior mediastinal shadow just above the clavicles with displacement of the trachea to the right.

Bilateral subtotal thyroidectomy was performed and the pathologist reported metastatic hypernephroma. Palliative tracheotomy also was done and she was treated with cobalt-60 beginning on the ninth day postoperatively. She was dismissed 49 days later with ingestion of 0.2 mg. L-thyroxine daily advised.

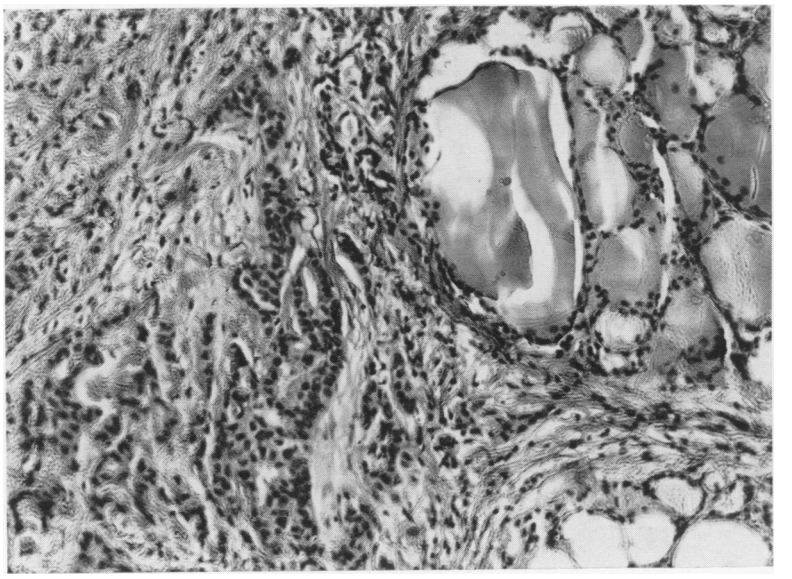

FIG. 5. (Case 11.) Section from thyroid showing metastasis from adenocarcinoma of the breast (hematoxylin and eosin; × 200).

The patient's family physician reported that nodules reappeared in the neck before she died, in October 1961.

Case 13. The patient, a 53-year-old man, came to this clinic in September 1962 because of hoarseness and a mass in the neck that had been present for five years. He had had left nephrectomy for Grade 2 hypernephroma in 1958 at another hospital.

On examination, a firm nodule, measuring 1.5 cm., was palpated on the isthmus of the thyroid, and right supraclavicular adenopathy was present. Thoracic roentgenograms revealed displacement of the trachea to the right.

Resection of the right lobe and isthmus of the thyroid gland was carried out and the pathologic report was multicentric, metastatic, Grade 2 hypernephroma. A tracheostomy tube that had been inserted during the surgical procedure was removed before his dismissal.

Case 14. A 51-year-old woman was seen at this clinic in December 1962, with a pea-sized right supraclavicular nodule of two weeks' duration. She had undergone left radical mastectomy for adenocarcinoma with positive axillary nodes in July 1961, and resection of the left lobe of the thyroid containing Grade 4 metastatic adenocarcinoma in October 1962. Enlarged left supraclavicular nodes had been excised in November 1962 and also contained Grade 4 metastatic adenocarcinoma. Each operation had been followed by cobalt-60 therapy. Histologic specimens obtained by the surgical procedures, which had been performed elsewhere, were received here for study and verification.

After evaluation of her condition here, she was sent home to be closely observed by her local physician. She returned in February 1963 complaining of hoarseness and increasing dyspnea on exertion. The left vocal cord was found to be fixed; thoracic roentgenograms revealed elevation of the left hemidiaphragm and free fluid in the left side of the thorax. A course of cobalt-60 therapy was administered to the mediastinum at this time and it was followed by symptomatic improvement.

When seen again in June 1963, the patient was found to have marked cervical adenopathy but no metastasis to bone. She was dismissed to the care of her family physician with the suggestion that hormonal therapy be tried to arrest further progression of the disease.

Comment

Carcinoma of the lung and malignant melanoma have been cited in the literature as two of the commonest primary sources of metastatic disease in the thyroid gland but both were absent from this series. In reporting a case of carcinoma of the rectum metastatic to the thyroid gland, Sklaroff noted that only four similar cases could be found in the literature up to 1954. One of our cases is included in his series.

The finding of hypernephroma as the commonest primary site of neoplasm is consistent with case reports in the literature of patients in whom metastatic disease was found in the thyroid gland on surgical exploration. Linton and co-workers mentioned that the sieve-like action of the lungs is an important factor in decreasing the number of tumor emboli which otherwise might lodge in the thyroid. A paradoxical metastasis seemed to be the only logical explanation of how metastatic cells could reach the thyroid until Batson showed that tumors of the thoracico-abdominal wall, breast, lungs, pelvis, and, occasionally, other organs have connections with the valveless vertebral system of veins and metastasize anywhere along the system without involving the portal, pulmonary, or caval systems.

More recently, Coman, Delong and McCutcheon studied the arterial transit of emboli originating in primary or secondary tumors of the lung, as well as those emboli that pass through the lungs. They injected suspensions of fixed and viable tumor cells from Brown-Pearce rabbit tumor into the left side of the heart of rabbits and found that the greatest number of tumors and emboli per square centimeter was found in the iris, pituitary, adrenals, and kidneys, while the smallest number was in muscle, thyroid, and splenic tissue. They concluded that embolic tumor cells are more likely to establish themselves and form new tumors if they lodge in capillaries, rather than in arterioles as occurs in the thyroid. These workers also observed that the embolic cells which are successful in establishing tumors are either single or in clusters tiny enough to penetrate into the capillary bed.

If a mass appears in the thyroid gland of a patient sometime after surgical excision of a hypernephroma or carcinoma of the breast, the possibility of a metastatic lesion should be considered in the differential diagnosis. On the other hand, if a clear-cell tumor is found microscopically in resected thyroidal tissue, the possibility of a primary neoplasm in the kidney must be entertained. However, Woolner and co-workers pointed out that some highly malignant primary thyroid carcinomas may present the appearance of a clear-cell tumor and, thus, occasionally simulate metastatic hypernephroma.

The long survival after thyroid operation in several of these cases lend support to the opinion of Elliott and Frantz that the slow course of hypernephroma warrants an aggressive policy of attack on the metastatic lesions. Moore and Walker reported a case of metastatic hypernephroma of the thyroid gland with subsequent thyroidectomy, nephrectomy, and resection of metastatic lesions in the lung. The same reasoning can be applied to such lesions in the thyroid arising from carcinomas in other sites.

Summary

Fourteen cases of carcinoma metastatic to the thyroid gland are described in which tissue diagnoses of both the primary neoplasm and the metastatic lesion in the thyroid were made. Two additional cases with no histologic confirmation of the primary tumor also are mentioned. In the 23-year period, 1940 through 1962, of 20,262 patients who underwent operation on the thyroid at the Mayo Clinic, 10 had proven malignant involvement of the thyroid gland. The average age in the series of 14 patients herein described was 55.7 years and the sex ratio was eight women to six men.

The primary lesion was hypernephroma in eight cases, adenocarcinoma of the breast in four cases, transitional cell tumor of the bladder in one case, and adenocarcinoma of the rectum in one case. Operation on the thyroid followed surgical treatment of the primary neoplasm in 12 cases, and the primary tumor was removed 11 days after thyroid operation in one case. In one case, necropsy revealed the primary tumor 1 day after thyroid operation.

The long survival after thyroid operation in several cases warrants a policy of aggressive attack on the metastatic lesions.

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